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Could psoralen plus ultraviolet A1 (“PUVA1”) work? Depth penetration achieved by phototherapy lamps

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Psoralen and ultraviolet A (PUVA) is useful in treating various hand and foot skin diseases.¹ Most cases of psoriasis respond well to phototherapy or PUVA. However, for some diseases, such as palmoplantar pustular psoriasis, PUVA is not always sufficient to produce therapeutic effect. If PUVA fails, it is sometimes necessary to progress to other treatments such as Grenz ray therapy (where available),² systemic retinoid or systemic immunosuppression. Could “PUVA1” (psoralen combined with ultraviolet A1 long wavelength ultraviolet A [UVA]) work in cases where conventional PUVA (psoralen plus broadband UVA) has been inadequate?

Previous *in-vitro* and *in-vivo* work has indicated that longer UVA wavelengths can activate Psoralen and induce erythema^{3,4}. Combine this with the fact that longer UV wavelengths penetrate deeper into tissue (and this is probably why UVA1 monotherapy might work in palmoplantar pustulosis⁵), and a potential result is that psoralen plus a UVA1 source might be more effective than the standard broadband UVA source in treating conditions that affect sites with a thick epidermis, such as palms and soles of

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feet.

We wanted to determine if PUVA1 might be a useful treatment, before deciding whether or not a pilot clinical study would be appropriate.

Monte Carlo radiative transfer (MCRT) methods use localised scattering and absorption probabilities to describe the path of photon packets through a medium, and are ideally suited to modelling a complex structure such as the upper layers of the skin⁶. These computationally intensive methods rely on repeated random sampling to form predictive models of radiation transport through a scattering medium, such as the skin⁷. MCRT methods are widely used and rely upon published optical properties of the tissue. Using a modified version of a previously published 5 layered MCRT skin model,⁸ irradiation by several phototherapy light sources (metal halide UVA1, fluorescent lamp UVA1, broadband UVA ("PUVA tubes") and narrowband ultraviolet B (a standard phototherapy) was simulated. Four simulations were performed, one for each light source, and each simulation was run with 100 million photon packets, to achieve statistically significant results. The total fluence, at depth, achieved by each light source is recovered. The four simulations were repeated for psoriatic skin, achieved by thickening the modelled stratum corneum (keratin layer of epidermis) by a factor of two.

The results of our simulations quantify the depth penetration advantage achieved by UVA1 (both fluorescent and metal halide lamps) over that achieved by broadband UVA and narrowband UVB. The advantage is smaller at 50% of incident fluence, but larger when considering the depth of 10% of the fluence (**Table 1**). In addition, we found that psoriatic tissue greatly reduced the depth achieved by all lamps - the stratum corneum strongly scatters and absorbs UV radiation, so thickening of this, by psoriatic scales, will greatly reduce the UV radiation reaching deeper layers of the skin. Given that the absorption spectrum of psoralen overlaps with the emission spectrum of UVA1 and the clinical evidence demonstrating the efficiency of longer wavelengths⁴ it may be possible to combine the two and achieve greater depth effect than with standard PUVA therapy. However as longer, less psoralen-effective wavelengths, reach the deeper depths, it is still not clear whether there will be enough activation of psoralen at deeper depths.

Following the example of Al-Ismail et al.⁴, at depth of 250 μm in healthy tissue, the Metal halide UVA1 source has a PUVA effective ratio of 0.207.

In conclusion, our results suggest that UVA1 radiation may be suitable for combination with psoralen in cases where deeper depth penetration is required than with conventional PUVA. However, this is dependent on how the penetrating UV radiation actually interacts with psoralen treated cells at depth within the skin and requires further investigation. We are planning a pilot study of PUVA1 in palmoplantar pustulosis.

Table 1. The results in Table 1 present the depth, measured from the surface of the skin, that 50% and 10% of the total integrated incident radiation has reached. **In addition, for the Metal Halide UVA1 lamp, we present the depths reached by 50% and 10% of the radiation in the wavelength bands comprising the lamp's output.**

Lamp	Healthy Skin		Psoriatic Skin	
	Depth Of 50% Incident	Depth Of 10% Incident	Depth Of 50% Incident	Depth Of 10% Incident
Broadband UVA (PUVA)	37 μm	215 μm	16 μm	65 μm
Narrowband UVB	17 μm	124 μm	14 μm	41 μm
Fluorescent UVA1	45 μm	254 μm	18 μm	83 μm
Metal Halide UVA1	46 μm	251 μm	19 μm	85 μm
340nm-350nm	33 μm	192 μm	16 μm	57 μm
350nm-360nm	39 μm	220 μm	17 μm	66 μm
360nm-370nm	43 μm	247 μm	18 μm	75 μm
370nm-380nm	47 μm	264 μm	19 μm	88 μm
380nm-390nm	49 μm	262 μm	20 μm	101 μm

390nm-400nm	51 μ m	257 μ m	20 μ m	102 μ m
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